

-continued

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19

1. A plurality of isogenic mammalian cells, wherein one or more endogenous glycogenes have been inactivated and/or wherein one or more exogenous glycogene have been introduced independently in individual cells of said plurality of mammalian cells.

2.-14. (canceled)

15. The plurality of isogenic mammalian cells of claim 1, furthermore encoding an exogenous protein of interest or induced to overexpress an endogenous protein of interest.

16.-18. (canceled)

19. The plurality of isogenic mammalian cells of claim 15, in which the protein of interest is a lysosomal enzyme expressed to comprise one or more posttranslational modifications independently selected from:

- a) with  $\alpha$ 2,3NeuAc capping,
- b) without  $\alpha$ 2,3NeuAc capping,
- c) with  $\alpha$ 2,6NeuAc capping,
- d) without  $\alpha$ 2,6NeuAc capping,
- e) without LacDiNac structure,
- f) high Mannose6phosphate,
- g) low Mannose6phosphate,
- h) without bisecting glycoforms; and
- i) with high mannose.

20. The plurality of isogenic mammalian cells of claim 1, wherein said one or more endogenous glycogene inactivated and/or exogenous glycogene introduced independently in individual cells of said plurality of mammalian cells is selected from the list of GNPTAB, GNPTG, NAGPA, ALG3/6/8/9/10/12s, Mannosidases (MAN1A1, MAN1A2, MAN1B1, MAN1C1, MAN2A1, MAN2A2), MOGS, GANAB plus MGAT1/2 and Sialyl transferases.

21. The plurality of isogenic mammalian cells of claim 1 wherein said one or more endogenous glycogene inactivated is GNPTAB, such as in order to increase sialic acids.

22. The plurality of isogenic mammalian cells of claim 19, wherein said lysosomal enzyme has obtained increased mannose-6-phosphate (M6P) tagging of N-glycans and/or has obtained changed site occupancy of M6P, such as by knocking out a gene selected from ALG3, ALG8, NAGPA.

23. The plurality of isogenic mammalian cells of claim 19, wherein said lysosomal enzyme has obtained increased high mannose structures, such as by knocking out a gene selected from MGAT1 and/or GNPTAB and/or MOGS.

24.-39. (canceled)

40. The plurality of isogenic mammalian cells of claim 1, wherein one or more of said cells has an inactivation and/or introduction of one or more glycogene selected from the list consisting of glycogenes associated with subset of O-Man-nose type glycoproteins (listed in Table 5 under group 1 genes for O-Glycans), such as POMT1 and/or POMT2 and/or TMTC1 and/or TMTC2 and/or TMTC3 and/or TMTC4 (Group 1).

41.-43. (canceled)

44. The plurality of isogenic mammalian cells of claim 1, wherein one or more of said cells has an inactivation and/or introduction of one or more glycogene selected from the list consisting of MGAT1 (N-Glycans), COSMC (O-GalNac), B4GALT7 (Glycosaminoglycans, GAG), B4GALT5/6 (Glycosphingolipids), POMGNT1 (O-Man) (Group 2).

45. (canceled)

46. The plurality of isogenic mammalian cells of claim 1, wherein one or more of said cells has an inactivation and/or introduction of one or more glycogene selected from the list consisting of MGAT2/3/4A/4B/4C/4D/5/5B, MAN1A1, MAN1A2, MAN1B1, MAN1C1, MAN2A1, MAN2A2, MOGS, GANAB, B3GALT1/T2/T4/T5, B3GALNT1/T2, B3GNT2/T3/T4/T6/T7/T8/T9, B4GALT1/T2/T3/T4, B4GALNT1/T2/T3/T4, GCNT1/T2/T3/T4/T6/T7, B3GAT1/T2, B4GAT1, LARGE, GYLT1B (LARGE2),